Q Connective tissue diseases:

1- Discoid LE
2- Clinical & histopathological criteria of DLE
3- Chronic DLE variants.
4- Histopathology of LE.
5- Management of DLE
6- Compare: DLE & SCLE.
7- SCLE
8- Major diagnostic criteria of SCLE.
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11- How to investigate lupus nephritis.
12- Neonatal LE.
13- Systemic sclerosis: etiopathogenesis, autoantibodies, DD
14- Cutaneous manifestations of dermatomyositis.
15- Nail changes in dermatomyositis.
16- Diagnosis & management of dermatomyositis
17- Serology of connective tissue diseases.
18- Raynaud's phenomenon.
19- Pathophysiology & management of mixed connective tissue disease.
20-Serology of mixed connective tissue disease
21- Major diagnostic criteria of mixed connective tissue disease

إجابة السؤال الأول والثاني

"① Discoid LE"
② Clinical & histopathological criteria for DLE

① epidemiology :-

age :- 20 - 40 years
sex :- more in females (2:1)
precipitating factors :- Trauma, infection, stress
sunburn, drugs (griseofulvin), also may start spontaneously
exacerbating factors :-
- Sunlight 70%
- Cold
- Premenstrual

② Clinical features :-

- well defined, erythmatous, discoid plaques
- with adherent scales & follicular plugging
- Healing occur with thin, white atrophic non contractile scar
- Neoplastic changes may occur (SCC or less frequently BCC)

③ Site :-

- Sun exposed areas e.g face (butterfly area)
- Scalp → causing a cicatrical alopecia
- Dorsa of hands
- V-area of neck & ears
- Mucous membrane (3%)
- Nail affection
- eye affection (conjuctival redness or ectropion)

Histopathology :-

① Hyperkeratosis with keratotic plugging
② Atrophy of stratum malpigii
③ Hydropic degeneration of basal cells
④ Thickening of basement membrane (PAS stain) (diagnostic)
⑤ patchy perivascular or periadnexal lymphocytic infiltrate.
⑥ odema, vasodilitation, extravasation of RBC's
⑦ Colloid bodies in upper dermis
⑧ pigmentary incontinence

Clinical Varities :-

① Localized DEE :- lesions on head & neck
② Disseminated DEE (generalized) :- above & below the neck
③ Hypertrophic (verrocus) DEE :- on arms, hands, nose & ears
④ palmoplantar erosive DEE
⑤ papular DEE :-
⑥ Rosea like DEE :- erythema & reddish nodules
⑦ Annular atrophic
⑧ Telangeatsic DEE
⑨ EE gyratums herpens

⑩ Lupus panniculitis :-
- firm asymptomatic "subcutanus nodules"
occur in DEE & SEE with normal overlying skin
- Healing occur with "cup shaped depress
site :- face, upper arms & upper trunk

(N.B) Some patients have discoid lesions overlying the panniculitis and this called "Lupus Profundus"

Histopathology of lupus panniculitis.

* most finding are present in the subcutaneous tissue
① predominant lobular lymphohistiocytic panniculitis
② vessel wall thickening
③ perivascular inflammatory infiltrate

(11) Lupus erythmetous tumidus

* Characterized by
  - induration & erythema
  - No scales
  - No follicular plugging
  - resolve spontaneously without scarring or atrophy.

* site: mostly on face

* Histopathology
  - intense dermal inflammatory infiltrate
  - Marked deposition of mucin

* DD: Differential Diagnosis
  - urticarial plaques described in lupus patients but Lupus tumidus → lesions are fixed.
  - Jessner's lymphocytic infiltrate

(12) Chilblain lupus (Lupus pernio)

- Dusky red or purple papules on the toes, fingers & sometimes the nose.
- lesions excerbated by moist cold climates,
- grossly & microscopic appearance like DLE
- tt → pentoxyfilin usual tt of DLE → ineffective

Diagnosis →

① History & Clinical examination

② Histopathology

③ Immunofluroscence (Lupus band test)

DIF → granular deposits of IgG at dermoepidermal junction in 75% of active lesions

- not in uninvolved skin

④ other lab examination

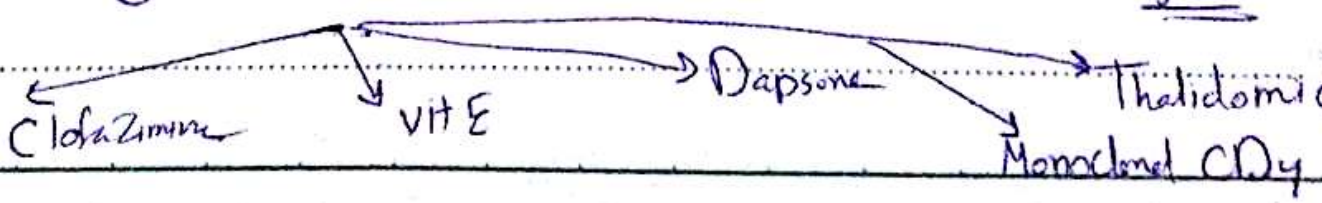
- ↑ ESR
- ↑ leucopenia
- +ve ANA in very few patients

DD

1. Actinic keratosis.
2. seborrheic dermatitis.
3. plaque psoriasis.
4. Polymorphic light eruption
5. lichen planus.

treatment.

1. avoid sunlight
2. Topical sunscreen
3. Topical steroid
4. intralesional injection of steroids
5. systemic treatment
   - (a) antimalarials
     - 200 - 400 mg/day
     - ophthalmogenic monitoring every 4-6 weeks
   - (b) systemic steroid (but should be limited to 4-6 weeks)
   - (c) systemic etretinate 1 mg/kg indicated in hyperkeratotic DLE
   - (d) in case of failure of steroid/antimalarial tt give



q6

	DLE	SCLE
CP	- Well-defined erythematous, discoid plaques with adherent scales & follicular plugging. - Healing →white, atrophic, non-contractile scar, slightly raised or hyperpigmented borders - Scarring alopecia - Sun exposed areas - MM, nail, eye affection	- Prominent photosensitive cutaneous lesions, non-scarring, papulosquamous or annular polycyclic lesions - Healing → grey-white hypopigmentation - Diffuse non-scarring alopecia - Photosensitivity 50% - Above the waist
HP	1- Hyperkeratosis with keratotic plugging 2- Atrophy of s.malpighii 3- Hydropic degeneration of basal cell 4- Thickening of BM 5- Patchy perivascular/periadnexal lymphocytic infiltrate 6- Edema, VD, ESR, colloid bodies in dermis	1- Hyperkeratosis & inflammatory infiltrate are less prominent 2- Hydropic degeneration & edema are more pronounced than DLE
Lab	1- DIF: granular deposits of IgG at DEJ 2- ESR ↑ 3- Leucopenia ↑ 4- +ve ANA in few cases	1- DIF: +ve 60% 2- ANA: +ve 60-80% 3- Circulating immune complexes 4- Anti-Ro, Anti-La Ab
ttt	1- Avoid PF 2- Topical sunscreen & steroid 3- Intralesional steroid 4- systemic: antimalarial- steroid Retinoid- thalidoamide- apsone	1- Avoid PF 2- Topical sunscreen & steroid 3- Systemic: antimalarial- steroid Retinoid- thalidoamide- apsone

(7) SCLE (sub acute cutaneous LE)

epidemiology :-

sex → female 3:1
age → adult
Course → less chronic
(more long lasting > ACLE)

atiopathogenesis

① genetic predisposition → evidence
- Famalial case
- Association with certain HLA types
- Role of auto antibodies →
anti-Ro / anti-La → in SCLE & neonatal L

② environmental factors →
- UV → strongest trigger
- Medications → (isoniazid, grisofulvin - dapsone) drug induced SCLE
- Virus inf → (eg herpes zoster)
- Trauma → (xray - burn, chemical)
- stress - cold
- seasonal exacerbation (summer)
- pregnancy, pre-menstrual

(2)

clinical features

- photosensitive eruption (confirmed to sun exposed skin)
- occur in 2 configurations
  ① annular / polycyclic (raised red border & clear centre)
  ② papulosquamous (with eczematous or psoriasiform appearance)
- heal with → hypo or depigmentation but do not scar

Relation to SLE → 10-15% (upto 50%) develope SLE

D.D ① PR ② Granuloma annulare ③ annular PS ④ Dermatitis atopic, contact ⑤ Erythema annulare centrifugum

serology: Anti Ro / SS-A autoantibodies → 80% of cases
anticardiolipin antibodies → 16%
- using human cell lines substrates → ANA homogenes 60%

histopathology

① Little or no hyperkeratosis follicular plugging, basement membrane Thickening, periadenexal infiltrate, or scaling

② sparse superficial lymphocytic infiltrate

③ More intense inflammation at dermal epidermal interface → severe hydropic degeneration → (more dermal edema)

evaluation and III

evaluation

① confirming the diagnosis
② search for systemic affection

III

① general measures
- photo protection → sunavoidance - protective clothing sunscreen

4

(2) Topical therapy

- Topical or intra lesional Corticosteroids ⟶ need to be high potency & limited to affected area.
- intra-lesional Triamcinolone ⟶ 4-5 mg/ml (inactive lesion discoid) may be repeated monthly.
- Topical immunomodulators ⟶ e.g (Tacrolimus)
- Topical retinoids

(3) systemic therapy

(a) anti-malarial therapy (gold standard (hydroxychlorquine - chloroquine - quinacrine)

(b) other systemic therapies ⟶ for anti malarial-resistant cutaneous lupus

- Immunosuppressive agents
- Thalidomide
- clofazimine
- sulfasalazine
- oral retinoids
- Dapsone

Q 8 | C.T

Q# Major diagnostic Criteria of SCLE

① Clinical ② HIP ③ Serological

① Clinical :→

① photosensitive : lesions are confined to sun exposed skin → sides of the face, V shaped area of necks, extensor aspects of upper extremities
• lesions may occur on the trunk (above the waist)

② lesions occur in either of 2 Configuration :→

ⓐ Annular "polycyclic" with raised red borders & central clearing

papulosquamous & an eczematous or psoriasiform appearance.

③ lesions heal with hypo- or- depigmentation But do not scar.

④ 10-50% of cases develop significant internal disease. Earthrites is the commonest feature but renal disease is mild & infreq

(2) (2)

(II) Histopathology: → SCLE characterized

(1) Little or no: hyperkeratosis, follicular plugging, basement membrane thickening, periadnexal infiltrate; deep dermal infiltrate or scarring.

(2) Sparse (no induration) superficial lymphocytic infiltrate.

(3) *Intense inflammation at the dermal-epidermal interface,
* more severe hydropic degeneration (up to formation of clefts & subepidermal vas. cels
* more pronounced dermal oedema

(III) Serology: →

(1) lupus band test: +ve in 60% of skin lesions & 25% +ve of normal skin.

(2) FANA → homogenous type in 60-80% of patients

(3) Anti-Ro antibodies in 80% & Anti-La antibodies in 30% of patients

Q Major & minor Criteria of SLE

according to (American Rheumatism Association)

4 Criteria for ID or more

1- Malar rash

2- Discoid LE Lesions

3- Photo sensitivity

4- oral ulcers

5- Non-erosive arthritis

6- Serositis :- pleuritis or peri carditis

7- Renal :- persistent proteinuria or Cellular Casts

8- Neuro Logical :- Seizures or psychosis.

9- Hemato Logical :- hemolytic anemia or leukopenia, Lympho penia, thrombo cyto penia

10- Immuno Logical :- anti-nDNA Abs anti phospho lipid
anti-Sm ab

11- Anti nuclear ab

Most diagnostic tests for SLE

1- Fluresent ANA test (indirect IF).

* (Screening) to rule in or out LE, the higher the titer, the more significad the test

2- Lupus band test (DIF).

* (more specific & sensitive)

← granular deposition of IgG, C_3, IgM at BMZ

in SLE then test is +ve in

Lesion — non lesion exposed to sun

IF test is +ve in non lesion, un exposed to sun

SLE — with renal affection

prognostic

3- LE cell test :- * (specific not v. sensitive)

← depend on ANA in serum of patient which cause invitro lysis of nuclear material which can be easily phagocytosed by neutrophils.
So LE cells is neutreuphils which have ingested basophilic homogenous nuclear material in presence of LE factor.

Q/ How to investigate Lupus nephritis ?

* Lupus nephritis (67 %)
  - very important in assessing the prognosis of LE.
  - Either focal or diffuse proliferative glomerulonephritis
    or
    membraneous lupus glomerulonephritis (nephrotic $)
    ⇓
    leading to chronic renal insufficiency with proteinuria & azotemia
  - the "wire loop" lesion of Lupus nephritis is due to subendothelial deposits of fibrinoid material.

* urine analysis: proteinuria 70.5 gm/day
  cellular casts.
  RBCs.

12.1

Neonatal lupus erythematosus (NLE)

- Neonatal form of SCLE may occurs in infants whose mothers have Anti-Ro autoantibodies

- SCLE-Like lesions - histologically identical to those of SCLE in adults

  Epidermal changes:

  * Little or no hyperkeratosis, basement membrane thickening, periadenexal infiltrate, follicular plugging, deep dermal infiltrate, or scarring

  * Superficial lymphocytic infiltrate sparse (no induration)

- Strong association ē <u>anti-Ro antibodies</u> (almost 100% of babies ē NLE have anti-Ro antibodies).

* Unlike SCLE in adults, lesions have apredilection for the <u>face</u> especially <u>periorbital</u> Region

* photosensitivity is very common in NLE, but sun exposure is not required for lesions to form = lesions may be present at birth)

12.2

* Resolve ē out scarring, although dyspigmentation may persist for many months & some children have residual telangiectasias.

* Internal manifestations (extra-cutaneous Findings)

1. Congenital Heart Block (ē or ē out cardiomyopathy)
   - ↳ almost always present by birth (rarely after birth)
   - ↳ Cardiac NLE has significant mortality (20%) & 2/3 of children require pacemakers

2. Hepatobiliary Diseases

3. Thrombocytopen

Both present at birth or may develop ē in the 1st few months of life

* Investigations in NLE

Children who have skin signs of NLE should be evaluated for internal manifestations ē physical examination in addition to an electrocardiogram
- ↳ Complete blood count
- ↳ Liver function tests.

* Neonatal L.E

- It occurs in female infants of mothers who have or will develop connective tissue disease
- The infant develops

(1) SCLE like lesions in the form of widespread, annular erythematous lesion, that develop within the first 2 months of life and improves in 4-6 months. periorbital "owl-eye" or "eye-mask", scalp and extremity are common sites, crusted lesions have been reported more in male infants.

(2) photosensitivity

(3) Transient thrombocytopenia

(4) Transient cholestatic hepatitis.

(5) Complete congenital heart disease block "permanent" which may

occur in the absence of disease

(6) Anti-Ro antibodies are present both in the infants and the mothers a serological marker that disappears by 4 to 6 months of age from the infants

(7) There is increased prevalence of HLA-DR3 and B8 in mothers of neonates with NLE.

* There is a strong inter-relation between all phenotypically different anti-Ro (SS-A) antibody the women However, all are at risk of giving birth to an infant with the NLE if the disease occurs during the childbearing years.

G13 Systemic Sclerosis. Etiopathogenesis autoantibodies PD.

Systemic Sclerosis: is a Systemic Autoimmune Connective tissue disease that affects the skin, blood vessels & internal organs.

- Skin → Fibrosis of skin
- Blood vessels → Raynaud's phenomena.
- organs → lung → Death, GIT

Aetiopathogenesis

1. Vascular Dysfunction
2. Immune activation
3. Tissue fibrosis

1. Vascular Dysfunction:

All Vascular tree affected (from Smallest Capillaries to large Pulmonary artery)

a sort of ischemia

Blood vessels changes: 1- decrease angiogenesis
2- endothelial cell injury.
3- Smooth muscle affected.
4- luminal occlusion → hypoxia → Collagen formation

Clinically → Raynaud's phenomena & Digital ulcers
(1) Reversible Vasospasm
(2) Irreversible arterial damage with lumen Proliferation & obstruction

→ Renal Crisis & pulmonary artery hypertension (large vessels affection)

No
Date

[2] Immune activation

- Both innate & acquired (B&T cells) play role.
- Specific Autoantibodies production.
  a) Anti-Centromere ⇒ (localized)
  b) Anti-topoisomerase I (Scl-70) ⇒ (Diffuse)

Others
- Anti-endothelial cell antibodies → trigger for cell apoptosis
- Autoantibodies against platelet-derived growth factor receptor

[3] Tissue Fibrosis

a) Excess deposition of Collagens, fibronectin
b) Role of Fibroblasts
   - Hypersensitivity of growth factors.
c) Role of cytokines & growth factor
   - Transforming growth factor B
   - Connective tissue growth factor

Autoantibodies

D.D الفرق الكوريتي ال

1) Elevate in Antinuclear antibodies (ANA)
   The Centromeric pattern (discrete speckled).
2) Antibodies to topoisomerase (Scl-70) ⇒ Specific to diffuse disease.
3) Anti Centromere antibodies ⇒ Specific for limited disease.

Q.1: (3)

No
Date

Differential Diagnosis

Systemic Sclerosis Distinguished by 3S → Symmetrical
→ Systemic affection
→ Serology +ve
→ Bilateral acral affection.

1) Mucinosis → Scleredema - induration of upper back, face & neck.
→ Scleromyxedema → waxy papules affect face, arms & thighs

2) Generalized morphea → No internal organ affection.

3) Carcinoma en Cuirasse → associated by metastatic Carcinoma (breast).

4) Drug or chemical-induced disorders:- Bleomycin.

5) Venous insufficiency - lipodermatosclerosis.

6) Chronic graft-versus-host disease.

7) Toxin-mediated disorders.

Q 14 (1)

Cutaneous manifestations of dermato-myositis

The cutaneous affection doesn't reflect the severity of the associated myositis.
About 1/3rd of Patients Present only with skin changes & characteristic muscle affection develop later (within 2 years).

The cutaneous lesions of dermatomyositis are often Pruritis. (Pruritis is a feature that can occasionally help distinguish dermato-myositis from L.E).

The Primary, classic skin lesion is a violaceous macular erythema distributed symmetrically. As the disease Progress the erythema may become Progressively Poikilodermatous & indurated, the latter secandary to mucin deposition.

A) Pathognomonic Signs:
occuring in 7a 1/2 of Patients

1- Gottron's Papules:
violaceous flat-topped papules overlying the dorsal inter-phalangeal or metacarpo-phalangeal, elbow or knee joints

Q 14 (2)

2- Gottron's Sign: Macular violaceous erythema with or without edema in the same distribution

B- other characterstic signs:

1- Periungual telengiectasia with ragged cuticle (Samitz sign) (non specific, may be found in other CTDs)

2- Heliotrope (violaceous) erythema (30-60%) of patients with slight edema affecting face especially the periorbital areas, upper chest & arms.

3- Poikiloderma (Poikilodermata myositis):
Distributed in a shawl distribution over the shoulders, arms & upper back.
* Poikiloderma of DM is violaceous while that of L.E is red.

4- Subcutaneous & peri-articular calcification if extensive, it is called "dystrophic calcinosis universalis" calcinosis is usually common in children & occurs more in the proximal muscles of shoulders & in pelvic girdle

5- Photosensitivity, fissured & scaly hands "mechanic's hands", acquired ichthyosis bullae & urticarial lesions. Pruritis is a common feature.

PROVEN LEGACY...
BETTER EFFICACY

Q 14 (3)

C) Uncommon Skin Features:

- Cutaneous erosions or ulcerations
- Holster sign (Poikiloderma of the lateral thighs)
- Flagellate erythema
- Vesicobullous lesions
- Exfoliative erythroderma
- Panniculitis
- Gingival telengiectasias
- Pustular eruption of the elbows & knees
- Lipoatrophy (Especially in Juvenile dermatomyositis)
- Small vessel vasculitis (especially in Juvenile dermatomyositis)

Q:15:- Nail changes in dermatomyositis?

Dilated capillaris of the nail folds, which are irregular, tortuous & easily visible.

Q 16:- Diagnosis & managment of dermatomyositis?

A. Diagnosis:-

1. Considering a patients' history, family, medical history.
2. Physical examination:-
   - Muscle & skin involvement.

Skin:- Rash, Gotton's papules, Dilated capillaris of the nail folds, hyperpigmentation, erythema of the scalp may occur, alopecia, red firm tender areas of panniculitis, Raynaud's phenomenon. Oedema of the eyelids, hands & arms.

Muscle:- - First patients notice aching, weakness & tenderness of the muscles which later shows atrophy.
- Difficulty of going up stairs or raising from a chair or difficulty in raising arms enough to comb the hair.
- There may be difficulty in speech & swallowing.
- Weakness of ocular muscles & respiratory difficulty.

3. Investigations:-
   1. Muscle biopsy & electromyography.
   2. Serum Creatine phosphokinase (CPK).
   3. Glutamic oxalacetic transaminase (SGOT) or aldolase (SPOT).

4. ↑ the 24-hour urinary creatine excretion.
5. ↑ ESR. 6. RF « Rheumatoid factor».
7. Anti-Jo-1, anti-Ku, anti-SRP antibodies.
8. Nuclear antigen M1-2 antibody.
9. Radiology shows widely scattered calcinosis in muscles & soft tissues.

B. Managment

After diagnosis is conferned:
- Rest is essential in the acute phase.
- Exclude internal malignancy in adults.
- Prednisolone 60-120 mg/day $\xrightarrow{\text{gradually reduce}}$ 5-10mg maintaus
- If no improvement è corticosteroids → Methylprednisolon 1g on 3 successive days. OR.
  Immunosuppressive is added:
  - Azathioprine - Methotrexate.
- Ciclosporin 5mg/Kg/day.
- Intravenous immunoglobulin combinedè ciclosporin
- Levamisole 600mg/week - Dapsone
- Treatment of calcinosis & other muscles d.

Q17-1 Serology of Connective tissue Ds ?

Serology → detection of blood + serum Antibodies

In SLE Serum autoantibodies reactive against Nuclear + Cytoplasmic Constituents

1) Antibodies against Nuclear Constituents
   - DNA
   - Histone
   - Small nuclear ribonuclear proteins SNRNP (Sm, La, nRNP)
2) Antibodies against cytoplasmic Constituents
   * Small cytoplasmic ribonuclear protein (Sc RNP)
   - Ro
   - La

- SLE → Direct IF (lupus band test) → detection of Ab in both involved and uninvolved skin • at DEJ around hair follicles • IgG • IgM Deposition
  +ve in 90% of involved skin
  +vein 70% of uninvolved sun exposed.
  +ve in 55% of uninvolved sun protected area.

→ Indirect IF : Fluorescent ANA test
  +ve [anti n DNA → peripheral ANA Pattern
  anti sm → speckled ~ ~
  anti nRNP → Nuclear ~ ~

- Drug induced LE → +ve Anti Histone Abs.

- SCLE
- Drug induced SCLE
- NLE

→ +ve anti cytoplasmic Ab.
• Ro : Cytoplasmic glycoprotein.
• La " Cytoplasmic RNA ptn.

- In SCLE → lupus band test +vein 60% of skin lession
  +ve in 25% of Normal skin.

- MCTD → IIF → +ve anti n RNP
  DIF → Epidermal nuclear IgG deposition.

DLE → -ve serology but anti Nuclear Abs in 30% of ptn
DIF → -ve in uninvolved skin

- CREST → +ve anti centromere Abs
- Diffuse cut SS → +ve anti Scl-70
- Morphea → +ve ant ss DNA in 50% of ptns
- Dermatomyositis :-
  - Dif → Globular deposition of IgM, IgA, C_3 in upper Dermis in $\frac{1}{3}$rd of Cases
  - Autoantibodies
    - a) Non myositis specific Abs
      - ANAs
      - Myositis & overlap syndromes have high ANA titre, anti RNP [PM + SLE or MCTD], anti PM-Scl [DM/PM + scleroderma], Anti Ku Abs [DM + SS]
    - b) Myositis specific Abs :-
      - Anti Jo-1 → against tRNA synthetase
      - anti SRP → against cytoplasmic ptns of signal recognition (specific for PM > particle
      - Mi-2 → against nuclear ptn Complex. "classical DM"
      - Anti MAS → against unidentified Cytoplasmic RNA "specific for PM"
      - Anti 3e, 155, KDa → in amyopathic DM.
- Antisynthetase syndrome → +ve Anti Jo-1

Serological tests used for Diagnosis & prognosis of CTD:

Raynaud's phenomenon

Def:

Episodic vasospasm of the digital arteries resulting in white, blue and red discoloration of the Fingers secondary to cold stimulus.

types:

① primary: No obvious arterial disease

② Secondary: Secondary to arterial disease

feature	primary Raynaud's	Secondary R
* Sex	F:M = 20:1	F:M = 4:1
* age of onset	puberty	>25 years
* Frequency of attacks	usually <5 per day	5-10 per day
* pre Cipitants	cold, emotional stress	Cold
* Ischemic injury	absent	present
* abnormal Capillaroscopy	absent	> 95%
* antinuclear antibody	absent / low titre	90-95%
* anti Centromere antibody	absent	50-60%
* anti-SCl-70 (topoisomerase I) antibody	absent	20-30%
* In vivo platelet activation	absent	> 75%

Differential diagnosis of Raynaud's phenomenon:-

① Structural vasculopathies:-
* Thoracic outlet Syndrome
* Takayasu's arteritis
* Buerger's disease
* Systemic sclerosis, SLE, DM, overlap Syndrome
* Cold injury, Vibration and Vinyl chloride

② abnormal blood elements:-
* Cryoglobulinemia, Cryofibrinogenemia
* Cold agglutinin disease
* Myeloproliferative disorders (eg. thrombocythemia)

③ abnormal vasomotion:-
* primary (Idiopathic) Raynaud's phenomenon
* Drug induced (ergot alkaloids - interferon - estrogen nicotine, cyclosporin, cocaine, Sympathomimetics)
* pheochromocytoma
* Carcinoid Syndrome

Treatment:-

① First line therapy:
avoid cold and tobacco products

② Second line therapy:
* vasodilators: Calcium channel blocker e.g nifedipine & angiotensin II receptor blockers e.g (Losartan) and phospho diesterase type 5 inhibitor e.g Sildenafil)

* Intravenous alprostadil (prostaglandin E1)
* Nerve blocks and Sympathectomies
* Anti platelet agents
* Topical preparation: ineffective

Q19 Pathophysiology & management of mixed Connective tissue disease (MCTD) ?

* Associated with HLA-DR4 and HLA_DR2

* Clinically: - Raynauds phenomenon 100%
  Sclerodactyly 90%
  Arthralgia 90%
  - Rare ⇒ esophageal dysmotility, pulmonary fibrosis renal affection.
  - there is good prognosis with long period of remission.

* DIF: Particulate epidermal nuclear IgG deposition.
* IIF: (FANA): speckled pattern.
* Serologically:
  - High titre of Anti_U1RNP antigen which is Sensitive to ribonuclease ~~Sm~~
  (in Contrast with that found in 25% of pts with SLE which is resistant to Ribonuclease "Sm")
  - -ve Anti n-DNA Abs. (Explain rarity of renal
  - -ve Anti-Sm Abs.

* treatment:
  - Prednisone 1mg/kg/day
  - Steroid sparing agent
  - Topical steroids.

Q: Serology of mixed connective tissue disease?

Serology:

1. high titres of anti-U_1RNp Abs (antibodies to ribonucleoprotein "U_1RNP" antigen which is sensitive to ribonuclease)
   It's characteristic to MCTDs

2. -ve Anti n-DNA Abs (explain rarity of renal disease)

3. -ve Anti-Sm Abs

CT (9) 20

1 →

* Serology of mixed Connective tissue disease ?

① * ANti U_1RNP Antibdies → high charcteristic (High titre)

② ANA → positive (100% of patient, high titre coarse speckled pattern)

③ anti-SM Abs → -ve

anti-dsDNA Abs → -ve

④ Rheumatoid factor → +ve in 50-70% of plent

⑤ Anti phospholipid Ab → +ve (less common than in SLE)

<u>athors</u> → CBC → Anemia + leucopenia

ESR → ↑ elevated

- Hypergammglubulinemia (poly)
- +ve Coombs test

Scanned by CamScanner

Q Major diagnostic criteria of mixed connective tissue diseases ?

* Mixed connective tissue diseases (MCTD) is clinical overlap syndrome with features of SLE, DM, scleroderma
* It's associated = HLA-DR2
HLA-DR4
* Diagnostic criteria:
① Serological:
- high titre of anti-U1 RNP (antibodies against ribonucleoprotein "U1 RNP" which is sensitive to ribonuclease"
② Clinical (3 of 5):
- Raynaud's phenomenon
- Sclerodactylyl
- Synovitis
- proven myositis (by histology)
- swollen hands / fingers
* diagnosis is made by (serology + at least 3 of 5 Clinical Criteria)